4-26-90

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

APR 26 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Review Revision For The Personal Protective Equipment Statements of Ronilan Fungicide.

To: James Stone/Susan Lewis, PM Team 21
Registration Division (H7505C)

From: Winston Dang, Ph.D., Chemist 4/16/90
Field Studies And Special Project Section
Non-Dietary Exposure Branch
HED(H7509C)

THRU: Alan P. Nielsen, Chief
Field Studies And Special Project Section
Non-Dietary Exposure Branch
HED(H7509C)

Charles Trichilo, Ph.D., Chief
Non-Dietary Exposure Branch
HED(H7509C)

HED Project #: 0-0548

RD or SRRD Record #: 258408, 258409

EPA Registration #: 7969-53, 7969-62

Caswell #: 323C

Registrant: BASF

Action Code: 300

Date Received: 1/26/90 Total Reviewing Time: 2 days

Deferral to: _____ Biological Analysis Branch/BEAD

_____ Science Analysis & Coordination Branch

_____ TB - Insecticide/Rodenticide Support Section

_____ TB - Herbicide/Fungicide/Antimicrobial

INTRODUCTION

Product: RONILAN^{R} WP, RONILAN^{R} FL

Active Ingredient: Vinclozolin, 50% in Ronilan WP, 41.3% in Ronilan FL

Background: Vinclozolin is used as a fungicide for strawberries and lettuce. The toxicity data of Vinclozolin is classified as Toxicity Category IV from the Acute Oral Toxicity study, LD_{50} > 10 g/kg (HDT) and is classified as Toxicity Category III for Acute Dermal Toxicity with LD_{50} > 2.5 g/kg (HDT). The latest studies in 1989 on oral developmental toxicity in the rats resulted in a NOEL of 15 mg/kg/day. The preliminary dermal developmental toxicity study indicates a NOEL of 60 mg/kg/day with a 26% dermal absorption rate.

ACTION REQUESTED

The Non-Dietary Exposure Branch(NDEB) has been requested to evaluate the amended personal protective equipment statements provided by the Registrant, BASF, dated 1/8/90 for their Ronilan fungicide products, Ronilan WP and Ronilan FL (EPA Reg. Nos. 7969-53 and 7969-62).

DETAILED CONSIDERATIONS

The preliminary dermal developmental toxicity study review was evaluated by D. Anderson of the Insecticide/Rodentcide Support Section of Toxicology Branch resulted in a NOEL of 60 mg/kg/day. Preliminary results from a percutaneous penetration study indicates that 26% of the dose applied is absorbed. Therefore, a dermal dose with a NOEL of 60 mg/kg/day is calculated to be equivalent to an oral dose of 15.6 mg/kg/day (= 60 x .26). These data show the consistency between oral developmental toxicity studies and the preliminary data from the percutaneous absorption study and the dose levels from the dermal developmental toxicity study. (personal communication with D. Anderson & see attachment #1)

COMMENTS AND RECOMMENDATIONS

New data gathered as per a protocol review by S. Knott of NDEB on 4/9/90 and 4/11/90 (see attachment #2 & #3) for proposed labeling and for measuring the human exposures resulting from the application of 50% Vinclozolin (HED # 0-1037) was evaluated. In his reviews, Knott indicates that, "The proposed label for

2

Ronilan WP does not mention any use of protective clothing in the Directions for Use".However, the amended labels provided from the Registrant, dated 1/8/90, have more detailed information in the personal protective equipment statements. NDEB accepts the concept of the revised labeling statements, but recommends that the wording be amended to say, "When applying this product - wear goggles or face shield, chemical resistant gloves, coveralls or long legged pants, socks, and long sleeved shirt. When mixing or loading or when adjusting, repairing or cleaning equipment wear chemical resistant gloves extending above the wrist, a chemical resistant apron, long legged pants, socks, and long sleeved shirt. Avoid breathing vapor or apray mist. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash before reuse."

cc: Circulation
Vinclozolin File
Correspondence
TB I/RS - D. Anderson

Attachment #1: Memo from D. Anderson of TB I to L. Pemberton of RD dated 3/30/90 (4 pages)
Attachment #2: Memo from S. Knott of NDEB to Rebecca Cool of RD dated 4/9/90 (2 pages)
Attachment #3: Memo from S. Knott of NDEB to Jim Stone of RD dated 4/11/90 (3 pages)

REVIEWER

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Attachment #1

MAR 29 90

Subject: EPA ID # 90-OR-08. Section 18 for the Use of Vinclozolin (Ronilan) on Snapbeans in Oregon.

Tox Chem No.: 323C.
Project No.: 0-0712A.
Record No.: 259731.

To: L. Pemberton/
Rebecca Cool PM 41
Registration Division (H7505C)

From: David G Anderson, PhD. David G Anderson 3/28/90
Section 2, Toxicology Branch I (IRS)
Health Effects Division (H7509C)

Thru: Marion Copley, DVM Marion Copley 3/29/90
Section Head, Section 2
Toxicology Branch I (IRS)
Health Effects Division (H7509C).

Attachment

CONCLUSIONS:

B. D. Wright, administrator of the Plant Division of the Oregon Department of Agriculture has requested a Section 18 Emergency Exemption for the use of Ronilan on snapbeans during the 1990 growing season. The Toxicology Branch 1 (IRS) has no objections to this request, provided a worker exposure assessment indicates a margin of exposure (MOE) of >100.[1] Previous Section 18's for the 1989 growing season were not supported, because: (1) New data demonstrating a NOEL of 15 mg/kg/day, (2) an unofficial estimate of exposure (using 100% absorption) indicated a potential worker hazard, and (3) dermal penetration estimates

[1] This MOE calculation should include an estimate of dermal penetration, previously unavailable. A dermal penetration of 26% can be assumed (Telephone call from Karen Blundell of BASF indicating a dermal absorption of 26%, 3/8/90). In addition, preliminary evaluation of dermal developmental toxicity studies recieved 3/20/90 (MRID # 414130-01) indicates excellent agreement (NOEL = 60 mg/kg/day) when the 26% dermal absorption is included in the calculations.

4

Primary reviewer: David G Anderson, PhD.
Section VII, Tox. Branch (H7509C).
Secondary reviewer: Marion Copley, DVM.
Section VII, Tox. Branch (H7509C).

Draft only

DATA EVALUATION REPORT

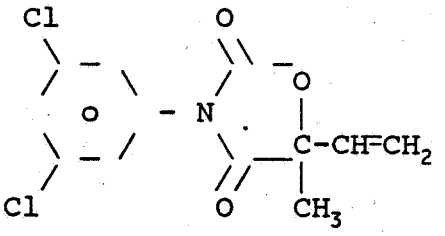
STUDY TYPE: Dermal Developmental Toxicity Study/83-3/Rat/34R0375/88074.

TOX. CHEM. No.: 323C

MRID No.: 414130-01.

TEST MATERIAL: Vinclozolin, technical; A.I. is [3-(3,5-dichlorophenyl)-5-ethenyl-5-methyl-2,4-oxazolidinedi-2,4-one].

STRUCTURE:



SYNONYMS: Ronilan 50W, 50% A.I., Ronilan FL, 41% A.I.

SPONSOR: BASF Corp. Chemicals Div., Ag. Chem., PO Box 13528 Research Triangle Park, NC 27709-3528.

TESTING FACILITY: BASF Aktiengesellshaft, Dept. Toxicology, 6700 Ludwigshafen, Federal Republic of Germany.

STUDY NO.: 34R0375/88074. Reg. Doc. No. BASF 90/0025.

REPORT TITLE: Study of Prenatal Toxicity of Reg. No. 83 258 in Rats After Dermal Application.

AUTHOR(S): Gelbke, H. P.

REPORT ISSUED: February 1, 1990.

CONCLUSIONS:
Doses Administered: 0, 60, 180, and 360 mg/kg/day, applied dermally to 25 Wistar [Chbb:THOM (SPF)] rats/group.

Preliminary Dermal Developmental Toxicity Study/83-3/ Rat/ 34R0375/88074.

Developmental Toxicity:
NOEL: 60 mg/kg/day.
LEL: 180 mg/kg/day for decreased anal-genital distance in males (pseudohermaphroditism). Possible increased incidence of dilated renal pelvis, and hydroureter in fetuses, but not in litters occurred at 360 mg/kg/day and higher.

Maternal Toxicity:
NOEL: 60 mg/kg/day.
LEL: 180 mg/kg/day for increases in absolute adrenal weights and at 360 mg/kg/day increases in absolute liver weights.

Core classification: Supplementary because stability data must be submitted (See section E. Additional Needed information at the end of this DER.)

D. DISCUSSION AND ABSTRACT:

Vinclozolin was administered dermally (vehicle water and 0.5% carboxymethylcellulose) to 25 rats/group at 0, 60, 180, and 360 mg/kg/day from gestational day (gd) 6 through 19. At gd 20 the fetuses were stated to be investigated by methods outlined in OECD and FIFRA guidelines. Marginal maternal toxicity was demonstrated by the statistically significant increase in absolute adrenal weight at 180 and 360 mg/kg/day. In addition, absolute liver weights were statistically significantly elevated at the same dose levels. No dose related gross abnormalities were noted in the kidneys, however, no histology was conducted on the organs. A statistically significant increase occurred during gd 13-15 in the body weight gain. The carcass weight and the body weight gain were all nominally elevated at 360 mg/kg/day over control values at gd 20. The body weight gain may have been test material related, but the effect was not statistically significant.

Male and female fetal body weights were not statistically significantly different from control values.

Pre- and post-implantation losses were nominally decrease and the number of live fetuses were nominally increased which are consistent with the statistically significant decrease in late resorptions at the 360 mg/kg/day dose level.

A statistically significant increase occurred in pseudohermaphroditism among male fetuses. The term pseudohermaphroditism was used to describe the effect because these males exhibited decreased anal-genital distances, but exhibited superficially normal internal testes. The anal-genital distance/body weight ratio in male fetuses was statistically significantly decreased at 180 mg/kg/day and higher. The response was dose related. These results are consistent with possible anti-hormonal effects from the test material.

Preliminary Dermal Developmental Toxicity Study/83-3/ Rat/ 34R0375/88074.

Soft tissue examination of fetuses indicated a statistically significant increased incidence in dilated renal pelvis and a nominal increase in hydroureter, but the effect was only nominally elevated in litters at 360 mg/kg/day and may not be dose related.

Skeletal examination of fetuses indicated increased incidence of variations and retardations (reduced sternebrae ossification) at 60 and 180 mg/kg/day but not at 360 mg/kg/day (Not dose related). There were no indications of an increased incidence of 14th rib in these studies as there had been in other oral studies (MRID # 411322-01) in the rat.

In summary, marginal effects occurred for increased soft tissue variations at 360 mg/kg/day(HDT) and statistically significant decreases occurred in the anal-genital distance in males at 180 mg/kg/day and above. The NOEL is 60 mg/kg/day. In the gavage study the effect level for these same effects is 50 mg/kg/day and the NOEL is 15 mg/kg/day. Preliminary results from a percutaneous penetration study indicates that 26% of the dose applied is absorbed. Thus, a dermal dose with a NOEL of 60 mg/kg/day is calculated to be equivalent to an oral dose of 15.6 mg/kg/day [(60 mg/kg/day) X (0.26) = 15.6 mg/kg/day], and a corresponding dermal LEL of 180 mg/kg/day is calculated to be equivalent to an oral dose of 46.8 mg/kg/day [(180 mg/kg/day) X (0.26) = 46.8 mg/kg/day]. These results indicate that the dose levels from the oral developmental toxicity studies are supported by the preliminary data from the percutaneous absorption study and the dose levels from the dermal developmental toxicity study. In addition, the NOEL and LEL for adrenal weight increase in this dermal developmental toxicity study is identical with the NOEL and LEL for the pseudohermaphrodism, respectively. Thus, adrenal steroidgenesis could be affected as well as hormal effects.

Attachment #2

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

APR -9 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Section 18 Requests from Wisconsin and Oregon for the use of Ronilan (FL and WP) on Snap Beans (HED # 0-0864).

TO: Rebecca Cool, PM 41
Registration Division (H7505C)

FROM: Steven M. Knott, Chemist
Environmental Chemistry Review Section
Non-Dietary Exposure Branch
Health Effects Division (H7509C)

THRU: Michael P. Firestone, Ph.D., Section Head
Environmental Chemistry Review Section
Non-Dietary Exposure Branch
Health Effects Division (H7509C)

Charles L. Trichilo, Ph.D., Chief
Non-Dietary Exposure Branch
Health Effects Division (H7509C)

INTRODUCTION

The Registration Division has requested that the Non-Dietary Exposure Branch prepare an exposure assessment for the use of Ronilan (Vinclozolin: 50% ai for WP and DF and 41.3% ai for FL) on snap beans. The assessment will be used to support a decision on Section 18 (Special Local Need) requests from the states of Wisconsin and Oregon.

CONCLUSION

NDEB has assessed mixer/loader and applicator exposure to Ronilan (WP,DF,FL) from use on snap beans. Ground application is assumed to be by ground boom equipment. The exposure estimates assume a 70 kg individual and have not been adjusted for dermal absorption. NDEB defers to Toxicology Branch II (HFAS) the adjustment of the dermal exposure estimates for dermal penetration and all margin of safety (MOS) calculations. The results of the exposure analysis are presented in the following two tables.

8

Exposure from Ground Boom Application

Formulation: Applicator	Application Rate (lb ai/Acre)	Exposure Mixer/Loader (mg/kg/day)	Exposure Applicator (mg/kg/day)	Combined (mg/kg/day)
WP:				
Private	0.75	0.084	0.102	0.186
	1	0.111	0.136	0.247
Commercial	0.75	0.204	0.25	0.454
	1	0.272	0.333	0.605
DF:				
Private	0.75	0.299	0.102	0.401
	1	0.399	0.136	0.535
Commercial	0.75	0.731	0.25	0.981
	1	0.974	0.333	1.307
FL:				
Private	0.62	0.247	0.084	0.331
	0.83	0.331	0.113	0.444
Commercial	0.62	0.604	0.206	0.81
	0.83	0.809	0.276	1.085

Exposure from Aerial Application

Formulation	Application Rate (lb ai/Acre)	Exposure Mixer/Loader (mg/kg/day)	Exposure Pilot (mg/kg/day)	Flagger (mg/kg/day)
WP	0.75	0.936	0.014	0.079
	1	1.25	0.019	0.105
DF	0.75	3.35	0.014	0.079
	1	4.46	0.019	0.105
FL	0.62	2.77	0.012	0.065
	0.83	3.71	0.016	0.087

Calculations for typical and maximum label application rates are provided (based on information obtained from BEAD). Open pour loading is assumed for the mixer/loader.

Labels for the different formulations did not accompany the request package from RD. However, review of a proposed BASF label for Ronilan WP (provided with a protocol submission) indicates that the labels may not provide enough information concerning the use of protective clothing. The exposure estimates assume that the mixer/loader is wearing a long sleeved

Attachment #3

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

APR 11 1990

7324

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: BASF Protocol for Study of Exposure to Workers Applying Ronilan WP (50 % Vinclozolin - HED # 0-1037).

TO: Jim Stone, PM 21
Registration Division (H7505C)

FROM: Steven M. Knott, Chemist
Environmental Chemistry Review Section
Non-Dietary Exposure Branch
Health Effects Division (H7509C)

Steven M. Knott

THRU: Michael P. Firestone, Ph.D., Section Head
Environmental Chemistry Review Section
Non-Dietary Exposure Branch
Health Effects Division (H7509C)

Charles L. Trichilo, Ph.D., Chief
Non-Dietary Exposure Branch
Health Effects Division (H7509C)

INTRODUCTION

BASF has submitted a mixer/loader/applicator exposure study protocol for Ronilan WP (50% vinclozolin). The following is NDEB's review and recommendations pertaining to the intended study.

CONCLUSION

NDEB has reviewed the subject protocol and found it to be unacceptable. The following concerns should be addressed.

1) Additional sites and replicates for ground boom and aerial applications are necessary.

2) The clothing scenario monitored must be representative of the clothing recommended on the pesticide label (see Attachment #2).

This label is pending registration in California.

Attachment 2.

BASF

Ronilan® WP

Fungicide

A wettable powder containing:

Active Ingredient	
3-(3, 5-Dichlorophenyl)-5-ethenyl-5-methyl-2,4-oxazolidinedione	50%
Inert Ingredients	50%

EPA Reg. No. 7969-53

KEEP OUT OF REACH OF CHILDREN.

CAUTION

Causes eye irritation. Do not get on skin, in eyes or on clothing.

Statement of practical treatment

If contacted, flush eyes immediately with water for 15 minutes. Get medical attention. In case of contact with skin or clothing, remove contaminated clothing, wash skin thoroughly with soap and water. This product is a potential skin sensitizer. If irritation persists get medical attention.

Environmental hazards

Do not apply directly to water. Do not contaminate water by cleaning of equipment or disposal of wastes.

Net contents 3 lbs.

(2 x 1½ lb. bags. Do not remove bags from carton except for immediate use.)

BASF Corporation Chemicals Division
100 Cherry Hill Road Parsippany, New Jersey 07054

Specimen Label

11

protection statements

Do not apply this product in such a manner as to directly or through drift expose workers or other persons, except those knowingly involved in the application. The area being treated must be vacated by unprotected persons.

Do not enter treated areas without protective clothing until sprays have dried.

Because certain states may require more restrictive re-entry intervals for various crops treated with this product, consult your State Department of Agriculture for further information.

Written or oral warnings must be given to workers who are expected to be in a treated area or in an area about to be treated with this product. Oral warnings must inform workers of areas or fields that may not be entered without specific protective clothing until sprays have dried, and appropriate actions to take in case of accidental exposure. When oral warnings are given, warnings shall be given in a language customarily understood by workers. Oral warnings must be given if there is reason to believe that written warnings cannot be understood by workers. Written warnings must include the following information: "WARNING. Area treated with Ronilan on (date of application). Do not enter without appropriate protective clothing until sprays have dried. If contacted, flush eyes immediately with water for 15 minutes. Get medical attention.

In case of contact with skin or clothing, remove contaminated clothing, wash skin thoroughly with soap and water. Call physician if irritation occurs. Wash contaminated clothing before reuse."

Directions for use

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

Storage and disposal

Do not contaminate water, food, or feed by storage or disposal.

Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility.

Completely empty bag into application equipment. Then dispose of empty bag in a sanitary landfill or by incineration, or, if allowed by state and local authorities, by burning. If burned, stay out of smoke.

In case of emergency

In case of large-scale spillage regarding this product, call:
CHEMTREC 800-424-9300
BASF Corporation .. 201-316-3000

In case of medical emergency regarding this product, call:

1. Your local doctor for immediate treatment.
2. Your local poison control center (hospital).
3. BASF Corporation 201-316-3000

All applicable directions, restrictions, precautions and Conditions of sale and warranty are to be followed. This labeling must be in the possession of the user at the time of application.

General information

Ronilan is a contact fungicide for the control of *Botrytis* fruit rot (gray mold) of strawberries, *Sclerotinia* "drop" (watery soft rot) of head lettuce, and brown rot blossom and twig blight, and fruit brown rot on stonefruit (see page 5 for list of stonefruit). Thorough coverage of plant parts to be protected is essential for effective disease control. If other diseases are a problem, an additional fungicide will be needed.

The repeated exclusive use of Ronilan, as is the case with the exclusive use of other fungicides, may result in the buildup of resistant strains of *Botrytis* and loss of disease control. A spray program alternating other fungicides with Ronilan may delay the buildup of resistant strains. If treatment becomes ineffective due to the presence of a Ronilan resistant strain of *Botrytis*, then prompt use of other fungicides is necessary to maintain disease control.

Strawberries

Time and rate of application for states other than California and Florida

Thorough spray coverage of the blossoms and developing fruit is essential. For full season control of *Botrytis* disease, the following spray program is recommended. The first application should be made no later than 10% primary bloom at rates indicated (see table). The interval between subsequent applications will vary according to weather conditions and resultant disease pressure. A rate of 1½ pounds product per acre is generally recommended. A one pound product per acre rate of Ronilan should be used only when low disease pressure can be predicted. A two pounds product per acre rate should be used when the foliage is dense and/or disease pressure is high. If a heavy rainfall occurs any time during this spray program or if a wet period (light rain, fog or dew) lasting more than 24 hours occurs, immediate retreatment is necessary at a rate of 1½ to 2 pounds product per acre as soon as conditions will allow the spray to dry on the plants.

12